

Therapeutic management of cervical condylomas and intra-epithelial neoplasms should be based on lesion size and distribution as determined by colposcopy and is not a function of cytohistologic grade or classification.

BARBARA WINKLER, MD  
JOEL PALEFSKY, MD  
San Francisco

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## Dilated Cardiomyopathy—Subcellular Mechanisms of Disease

TO CLARIFY CONCEPTS about heart muscle disease, the World Health Organization and The International Society and Federation for Cardiology jointly defined cardiomyopathy as heart muscle disease of undetermined etiology. The uniform use of such classification and terminology may help clarify the multiple and complex disorders that have been included in a less restricted definition. Arguments still exist that suggest returning to the use of the term cardiomyopathy in its broadest sense, which could include the etiology of the heart muscle disease within the term. Irrespective of the classification or use of terminology, the common postmortem findings in such heart muscle disease are strikingly similar: characteristic cardiomegaly, globoid heart with left ventricular dilation and associated findings suggesting congestive heart failure.

Classifications alone do not help greatly in understanding the subcellular nature of intrinsic heart muscle disease. In similar ways, the cell biology of the failing myocardium is poorly understood. A growing body of evidence suggests progress in understanding some cell biologic and biochemical adaptive compensations in the cardiac myocytes under the influence of thyroid hormone excess or deficiency. In such conditions, alterations in thick filament function may relate closely to changes in quantity and distribution of cardiac myosin isoforms present in the cardiac myocytes.

Analogous evidence does not exist for relating myocardial contractile changes in dilated cardiomyopathy to the thick filament. An *in vitro* model of doxorubicin (Adriamycin) heart muscle disease has recently been created using cultured neonatal rat cardiac myocytes (CMC) in which CMC are treated with doxorubicin hydrochloride *in vitro*. Myocardial contractile protein synthesis was monitored with attention focused on actin, particularly  $\alpha$ -actin, which is the isoform present in the cardiac thin microfilament.

A dose-dependent decrease in CMC protein synthesis and particularly of cardiac  $\alpha$ -actin was seen in CMC administered micromolar doxorubicin. Lower doxorubicin concentrations did not cause this effect on cardiac  $\alpha$ -actin synthesis. This *in vitro* observation may relate to the loss of contractility seen in doxorubicin-induced heart muscle disease *in vivo*. As sophisticated cell and molecular biologic techniques become available to cardiovascular research, the understanding of contractility defects of intrinsic heart muscle disease may rely

less heavily on classification or morphologic observation and more heavily on the nature of the biochemical defect leading to the contractile failure.

WILLIAM LEWIS, MD  
Los Angeles

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## The Use of Fresh Frozen Plasma—Indications and Risks

FRESH FROZEN PLASMA is the liquid portion (200 to 250 ml) of one unit of whole blood that has been separated and frozen within six hours after donation. It contains the labile and stable components of the coagulation system, components of the complement and fibrinolytic systems, albumin, immunoglobulins and all other plasma proteins and nutrients. One ml of fresh frozen plasma contains about one unit of coagulation factor activity; each bag contains about 400 mg of fibrinogen.

During the past decade, the use of fresh frozen plasma has increased tenfold. Each year in the United States, 700,000 patients receive almost 2 million units of fresh frozen plasma, despite few established indications for its use. About 20,000 to 70,000 cases of viral hepatitis may be transmitted annually through its use. Additional risks include transmission of other infectious diseases, anaphylactoid or other allergic reactions, alloimmunization and volume overload.

In September 1984, the National Institutes of Health and the Food and Drug Administration sponsored a conference to examine the issues and increasing professional concerns about the indications, effectiveness and safety of the use of fresh frozen plasma. One conclusion was that 90% of its current use is inappropriate. Specifically, it was stressed that there is no justification for the use of fresh frozen plasma as a volume expander or as a nutritional source since safer alternative therapies exist. The following current clinical indications for use were recommended:

- Replacement of isolated factor deficiencies for factors II, V, VII, IX, X or XI when specific component therapy (factor concentrate) is neither available nor appropriate.
- Replacement of multiple coagulation factors in patients with liver disease or consumptive coagulopathies. The efficacy, however, of administering fresh frozen plasma to patients with coagulopathy related to liver disease has not been clearly defined.
- Reversal of warfarin sodium effect. Fresh frozen plasma replaces the vitamin K-dependent coagulation factors (II, VII, IX and X; proteins C and S) when anticoagulated patients are actively bleeding or require an emergency operation.
- Massive blood transfusion (greater than one blood volume within several hours). The use of fresh frozen plasma in cases of massive blood transfusion has greatly increased in the past decade, possibly due in part to a relative unavailability of whole blood. Hemorrhage in a massively transfused patient is caused more frequently by thrombocytopenia than by coagulation factor "wash-out." The use of plasma to re-